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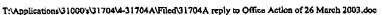
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Cheng et al. App. No. 10/081,969

## IN THE CLAIMS

As set forth below, please amend claims 4, 10, 11, 13, 18-25, 27, 29-32, 34-37, 44, 45, and 47; cancel claims 12, 15, 46, 52-57, and 60; and add new claims 61-66.

- 1. (Original) A recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR.
- 2. (Original) The recombinant viral vector of claim 1, wherein the termination signal sequence is the SV40 early polyadenylation signal sequence.
- 3. (Original) The recombinant viral vector of claim 1, wherein the E2F responsive promoter is the human E2F-1 promoter.
- 4. (Currently Amended) The recombinant viral vector of claim 1, wherein the adenoviral nucleic acid backbone is derived from an adenovirus serotype 5 (Ad5) or serotype 35 (Ad35) backbone.
- 5. (Original) The recombinant viral vector of claim 1, wherein the gene essential for replication is the E1A gene.
- 6. (Original) The recombinant viral vector of claim 1, further comprising a deletion upstream of the termination signal sequence.
- 7. (Original) The recombinant viral vector of claim 6, further comprising a deletion between nucleotides 103 and 551 of the adenoviral type 5 backbone or other corresponding bps of other Adenovirus serotypes.
- 8. (Original) The recombinant viral vector of claim 1, further comprising a mutation or deletion in the E3 region.
- 9. (Original) The recombinant viral vector of claim 5, further comprising a tissue-specific promoter operably linked to E4.



- 10. (Currently Amended) The recombinant viral vector of claim 9, wherein said tissuespecific promoter is derived from the a human telomerase reverse transcriptase promoter.
- 11. (Currently Amended) The recombinant viral vector of claim 9, wherein said tissue-specific promoter is the Trtex promoter of SEQ ID NO:94 or the TERT promoter of SEQ ID NO:93.
- 12. (Cancelled)
- 13. (Currently Amended) The recombinant viral vector of claim 9, wherein said tissue-specific promoter is derived from the an osteocalcin promoter.
- 14. (Original) The recombinant viral vector of claim 8, wherein the E3 region has been deleted from said backbone.
- 15. (Cancelled)
- 16. (Original) The recombinant viral vector of claim 1, further comprising a mutation or deletion in the E1b gene.
- 17. (Original) The recombinant viral vector of claim 16, wherein said mutation or deletion results in the loss of the active 19kD protein expressed by the wild-type E1b gene.
- 18. (Currently Amended) The recombinant viral vector of claim 1, further comprising a coding sequence of interest therapeutic gene.
- 19. (Currently Amended) The recombinant viral vector of claim 18, wherein said therapeutic gene coding sequence of interest is inserted in the E3 region.
- 20. (Currently Amended) The recombinant viral vector of claim 19, wherein said therapeutic gene coding sequence of interest is inserted in place of the 19kD or 14.7 kD E3 gene.
- 21. (Currently Amended) The recombinant viral vector of claim 18, wherein said therapeutic gene is coding sequence of interest encodes an immunostimulatory gene protein.
- 22. (Currently Amended) The recombinant viral vector of claim 21, wherein said immunostimulatory gene protein is a cytokine.

23. (Currently Amended) The recombinant viral vector of claim 21, wherein the immunostimulatory gene protein is selected from the group consisting of GM-CSF, IL1, IL2, IL4, IL5, IFNα, IFNγ, TNFα, IL12, IL18, and flt3.

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- 24. (Currently Amended) The recombinant viral vector of claim 21, wherein said immunostimulatory gene protein is selected from the group consisting of MIP1α, MIP3α, CCR7 ligand, calreticulin, B7, CD28, MHC class I, MHC class II, and TAPs.
- 25. (Currently Amended) The recombinant viral vector of claim 21, wherein said immunostimulatory gene protein is a tumor associated antigen.
- 26. (Original) The recombinant viral vector of claim 25, wherein said tumor associated antigen is selected from the group consisting of MART-1, gp100(pmel-17), tyrosinase, tyrosinase-related protein 1, tyrosinase-related protein 2, a melanocyte-stimulating hormone receptor, MAGE1, MAGE 2, MAGE 3, MAGE 12, BAGE, GAGE, NY-ESO-1, β-catenin, MUM-1, CDK-4, caspase 8, KIA 0205, HLA-A2R1701, α-fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic protein, p53, Her2/neu, triosephosphate isomerase, CDC-27, and LDLR-FUT.
- 27. (Currently Amended) The recombinant viral vector of claim 21, wherein said immunostimulatory gene protein is an antibody that blocks inhibitory signals.
- 28. (Original) The recombinant viral vector of claim 27, wherein the inhibitory signal is due to expression of CTLA4.
- 29. (Currently Amended) The recombinant viral vector of claim 18, wherein the therapeutic gene is coding sequence of interest encodes an anti-angiogenic gene protein.
- 30. (Currently Amended) The recombinant viral vector of claim 29, wherein said antiangiogenic gene protein is selected from the group consisting of a VEGF/VEGFR antagonist, an angiopoietin/Tie antagonist, an Ephrin/Eph antagonist, and an FGF/FGFR antagonist.
- 31. (Currently Amended) The recombinant viral vector of claim 29, wherein said antiangiogenic gene protein is an inhibitor of PDGF, TGFβ, or IGF-1.

- 32. (Currently Amended) The recombinant viral vector of claim 29, wherein said antiangiogenic gene protein is a fragment of an extracellular matrix protein.
- 33. (Original) The recombinant viral vector of claim 32, wherein said extracellular matrix protein is selected from the group consisting of angiostatin, endostatin, kininostatin, fibrinogen-E, thrombospondin, turnstatin, canstatin, and restin.
- 34. (Currently Amended) The recombinant viral vector of claim 29, wherein the antiangiogenic gene protein is a fragment of TrpRS.



- 35. (Currently Amended) The recombinant viral vector of claim 29, wherein the antiangiogenic gene protein is selected from the group consisting of sFlt-1, sFlk, sNRP1, sTie-2, IP-10, PF-4, Gro-beta, IFN-gamma (Mig), sEphB4, sephrinB2, vasostatin, PEDF, prolactin fragment, proliferin-related protein, METH-1, and METH-2.
- 36. (Currently Amended) The recombinant viral vector of claim 18, wherein said therapeutic gene is a suicide gene coding sequence of interest encodes a protein that leads to cell death.
- 37. (Currently Amended) The recombinant viral vector of claim 36, wherein said suicide gene protein that leads to cell death is selected from the group consisting of CPG2, CA, CD, cyt-450, dCK, HSV-TK, NR, PNP, TP, VZV-TK, and XGPRT.
- 38. (Original) The recombinant viral vector of claim 1, wherein said recombinant viral vector is capable of selectively replicating in and lysing Rb-pathway defective cells.
- 39. (Original) The recombinant viral vector of claim 38, wherein tumor-selectivity is at least about 3-fold as measured by E1A RNA levels in infected tumor vs. non-tumor cells.
- 40. (Original) A recombinant viral vector comprising an Ad5 nucleic acid backbone, wherein said backbone comprises in sequential order: a left ITR, an SV40 early polyA site, a human E2F-1 promoter operably linked to the E1A gene, an adenoviral packaging signal, and a right ITR.
- 41. (Original) The recombinant viral vector of claim 40 further comprising a deletion between nucleotides 103 and 551 of the adenoviral backbone.

- 42. (Original) The recombinant viral vector of claim 40 further comprising a mutation or deletion in the E1b gene, wherein said mutation or deletion results in the loss of the active 19kD protein expressed by the wild-type E1b gene.
- 43. (Original) The recombinant viral vector of claim 40, further comprising a tissue-specific promoter operably linked to E4.
- 44. (Currently Amended) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is derived from the a human telomerase reverse transcriptase promoter.
- 45. (Currently Amended) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is the <u>a</u> Trtex promoter.
- 46. (Cancelled)
- 47. (Currently Amended) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is derived from the an osteocalcin promoter.
- 48. (Original) An adenoviral vector particle comprising the viral vector of claims 1.
- 49. (Original) The adenoviral vector particle of claim 48, further comprising a targeting ligand included in a capsid protein of said particle.
- 50. (Original) The particle of claim 49, wherein said capsid protein is a fiber protein.
- 51. (Original) The particle of claim 50, wherein said ligand is in the HI loop of said fiber protein.
- 52. (Cancelled)
- 53. (Cancelled)
- 54. (Cancelled)
- 55. (Cancelled)
- 56. (Cancelled)

- 57. (Cancelled)
- 58. (Original) The vector of claim 1, wherein said backbone comprises a gene of the E3 coding region.
- 59. (Original) The vector of claim 58, wherein said gene is selected from the group consisting of E3-6.7, KDa, gp19KDa, 11.6KDa (ADP), 10.4 KDa (RIDα), 14.5 KDa (RIDβ), and E3-14.7Kda.
- 60. (Cancelled)
- 61. (New) A recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises a heterologous termination signal sequence downstream of the left ITR.
- 62. (New) The recombinant viral vector of claim 61, comprising a heterologous transcriptional regulatory sequence operably linked to the coding region of a gene that is essential for replication of said vector, wherein the termination signal sequence is upstream of the heterologous transcriptional regulatory sequence.
- 63. (New) The recombinant viral vector of claim 62, wherein the gene essential for replication is the E1A gene.
- 64. (New) The recombinant viral vector of claim 61, wherein the termination signal sequence is an SV40 polyadenylation signal sequence.
- 65. (New) The recombinant viral vector of claim 62, wherein the heterologous transcriptional regulatory sequence is an E2F responsive promoter
- 66. (New) The recombinant viral vector of claim 65, wherein the E2F responsive promoter is upstream of the E1A transcription unit.

